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THE PREVENTION OF CANCER

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Clinical Aspects

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CHAPTER 3

FOOD

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INTRODUCTION

The general public are aware that some constituents of foods and beverages may cause cancer. However, their fears are associated more with man-made chemicals than with the naturally occurring constituents of food. There is a tendency to regard 'natural' foods as without possibility of danger. This view is basic to many of the organizations or protagonists of 'natural' and 'health' foods. In the present chapter the scientific basis for these fears and attitudes is considered from a rational viewpoint.

The processing of food, particularly with a view to its preservation, is by no means a recent development. Some current preservative methods were known in ancient times, for example, the dehydration of cereals and fruits, the drying and smoking of fish and meat, and storage in brine and alcohol, and natural products have always been used to flavour food.

The increase in world population is closely linked with increased efficiency in the production of food. Advances in chemical and biological knowledge, the widespread use of agricultural chemicals and preservatives, together with new engineering processes, have made the control of standardized food products possible. As a result, more food, of a better quality, is produced, and to abandon modern processing methods now would certainly lead to world-wide famine. This argument, however, does not apply to the use of food flavours and colours. These are often without preservative or nutritional value and are present only to make food more acceptable to a society conditioned by competitive advertising to expect processed food to be of a standard flavour and colour.

The public mistrust of food-processing in relation to cancer has been caused mainly by the use of cheap substitutes in food. If raspberry pips in jam are really tiny chips of wood, what else is not what it seems? Doubts are raised concerning the origin of colour and flavour, and whether substitute constituents have been tested for cancer hazard.

Enough is known to be fairly confident that no potent carcinogens are added to foodstuffs in Great Britain. Stringent tests are carried out on new food additives, but many traditional processes, additives and 'natural' foods have not been adequately tested for possible carcinogenic effects.

In both Great Britain and the United States of America there has been a declining incidence of gastric cancer during the past 50 years. This suggests that modern hygienic processing methods reduce rather than increase the cancer hazard from food. However, cancer of any site in the body may be induced by chemicals in food and complacency is not justified. Mortality from cancer of the colon has changed little in the last 50 years: either the

introduction of new hazards is balanced by the elimination of the old ones, or exposure to the old hazards has not changed, or hazards in food are not implicated.

CLASSIFICATION OF POTENTIAL CANCER HAZARDS FROM FOOD

(1) *Constituents of natural foods* (for example: major constituents, such as cycasin and bracken; minor constituents, such as safrole and citrus oils; breakdown products due to ripening or general decay; carcinogenic constituents produced by contamination with specific microbes and the production of toxins by them, such as aflatoxin, toxins produced by *Penicillium islandicum*).

(2) *Carcinogens introduced during cooking* (for example, carcinogens produced by the overheating of fats; 3,4-benzpyrene in smoked foods, coffee and charcoal steaks, and so on).

(3) *Contamination of foods with man-made chemicals* (for example: insecticides, such as DDT, aldrin, dieldrin and aramite; herbicides; fertilizers; hormones, such as oestrogens; antibiotics; detergents; metals, such as tin, lead, selenium, and so on).

(4) *Chemicals used in food preservation and processing* (for example: stabilizers; anti-oxidants; anti-foaming agents; emulsifiers; dispersing agents; preservatives).

(5) *Substances added deliberately to food for purposes of flavour or colour* (for example: sweeteners such as dulcin, saccharin and cyclamates; numerous other flavours; colours such as butter yellow, ponceau 3 Rand blue VRS).

(6) *Carcinogens introduced into food as a result of sterilization by ionizing radiation*

There is insufficient space for detailed consideration of the thousands of substances which may be present in food, naturally, as deliberate additives or as a result of contamination. Therefore, consideration is restricted to a few substances where either carcinogenicity is suspected, or because they illustrate particular problems.

DETAILED CONSIDERATION OF CERTAIN FOOD CONSTITUENTS

Natural Foods

Cycads

In tropical countries plants of the cycad family constitute an important source of dietary starch. The potential toxicity of cycad products is recognized by the natives of these countries, who use elaborate preparative methods to remove toxins.

Laqueur and colleagues (1963) fed flour prepared from the nuts of *Cycas circinalis L.* to rats in an investigation of amyotrophic lateral sclerosis amongst Guam islanders. Evidence of neurotoxicity was seen but several of the rats also developed benign and malignant tumours of the liver and kidney. Mickelsen and colleagues (1964) observed cirrhosis occlusion of vessels in the liver, gastro-enteritis and nephritis in pigs, horses and cattle fed cycad meal.

In 1960, Nishida, Nagahama and Numata discovered in cycad meal the

presence of cycasin, a glycoside with a nitrosamine-like structure known to be hepatotoxic (Nishida and colleagues, 1956). Kobayashi and Matsumoto (1964) suggest that the proximal carcinogen is not cycasin but one of its metabolites, methylazoxymethanol.

Essential Oils

Roe and Field (1965) reviewed literature concerning the toxicity, including carcinogenicity, of the essential oils. Natural and synthetic essential oils are used widely as a flavour or odoriferous principle in food, drugs and cosmetics, and certain of these oils have shown carcinogenic or tumour-promoting activity in experimental animals.

Citrus oils—Following a single subcarcinogenic dose of a carcinogenic polycyclic hydrocarbon, repeated applications of various citrus oils promoted the development of skin tumours in mice (Roe and Peirce, 1960). Further tests on lime oil revealed similar promoting activity for the epithelium of the forestomach of mice (Field and Roe, 1965). Because of anatomical differences between mouse and man, and because the doses used in experiments were large, the results do not imply that citrus oils constitute a serious cancer hazard. However, they suggest that the practice of preparing citrus drinks by pulverizing the entire fruit may not be without danger.

The only epidemiological study in which citrus oils are specifically mentioned is that of Wynder and Bross (1961), who found no correlation between oesophageal cancer and consumption of citrus fruits.

Safrole—Safrole, a major constituent of Sassafras oil, found also in star anise, camphor oil, nutmeg and cinnamon leaf oils, is used as a flavouring agent in root beer, chewing gum, toothpastes and certain pharmaceutical preparations. Homburger and colleagues (1961) and Long and colleagues (1963) reported the induction of cirrhosis and liver cancers in rats fed a diet containing safrole. The possibility that it is carcinogenic in man has not been investigated.

Bracken

Bracken is eaten by cattle and is recommended for human consumption by protagonists of 'natural' foods. Evans and colleagues (1954; 1958) reported pyrexia, bone marrow change, widespread petechial haemorrhages and ulceration of the gut in cattle following ingestion of *Pteridium aquilinium.* When implanted intravesically, an extract of urine from bracken-fed cattle induced haemangiomatous lesions in dogs (Georgiev and colleagues, 1963) and in mice (Pamukcu, 1965). Evans and Mason (1965) reported adenomas and adenocarcinomas of the intestinal tract in bracken-fed rats.

Caffeine

The fact that caffeine is mutagenic (Fries and Kihlman, 1948; Andrew, 1959) gives some credence to the possibility that it is also carcinogenic. However, Goldstein and Warren (1962) found no evidence of a correlation between caffeine consumption and cancer of the stomach or colon in a small epidemiological survey.

Aflatoxins

In 1960 some 100,000 young turkeys died after being fed mashes containing ground-nut meal imported from Brazil. It transpired that the nuts from which the meal was prepared had been infected with a mould, *Aspergillus flavus*, which produces a group of toxic principles, including aflatoxins B and G.

Doses of aflatoxins as small as 20 μg kill young ducklings within a few days, and striking pathological changes are found in the liver. Other species are not so sensitive to the acute toxic effects but slowly develop liver damage and liver and kidney tumours after exposure. Lancaster, Jenkins and Philp (1961) saw liver tumours, whilst Salmon and Newberne (1963) and Le Breton, Frayssinet and Boy (1962) saw both liver tumours and kidney adenomas in rats fed toxic ground-nut meal. Dickens and Jones (1963; 1965) recorded subcutaneous sarcomas at the site of injection of aflatoxins into rats and mice. Tulpule, Madhavan and Gopalan (1964) and Madhavan, Tulpule and Gopalan (1965) recorded acute liver damage and hepatic fibrosis in monkeys given aflatoxin by stomach tube.

Man is undoubtedly exposed to aflatoxin: toxin-producing strains of *A. flavus* have been found in ground-nuts all over the world (Allcroft and Carnaghan, 1963) and in other human foodstuffs such as maize (Allcroft and Carnaghan, 1963), cotton-seed cake (Loosmore and colleagues, 1964) and peas (Spensley, 1963). Ambrecht and colleagues (1963) found that the fungus would grow and produce toxin in rye, soya beans, rice, oats and buckwheat. Golberg (1962) pointed out that *A. flavus* has been added to sauces, particularly those containing soya bean flour, because the mould acts as a source for certain hydrolytic enzymes.

At present, the carcinogenicity of aflatoxin for man is not proved. In Western industrialized countries where primary cancers of the liver and kidney are uncommon, it is unlikely that aflatoxin is important as a human carcinogen. However, in many tropical and under-developed countries liver cancer is common and aflatoxin may be an important factor. The Bantu, amongst whom liver cancer is common, brew alcoholic beverages from various cereal crops; and Golberg (1962) suggested that *A. flavus* may be one of the moulds involved in the brewing process (*see* Chapter 16 for further discussion on the subject). Combined microbiological and epidemiological surveys now in progress should indicate the extent of the possible carcinogenic activity of the toxins from *A. flavus* and related moulds.

Penicillium islandicum Toxins

In Japan, rice infected with the mould *Penicillium islandicum* has given rise to acute liver damage in man and animals (Uraguchi and colleagues, 1961). Rats fed extracts of the same infected rice developed liver cancer (Kobayashi and colleagues, 1959).

3,4-Benzpyrene and other Carcinogens in Uncooked, Cooked and Smoked Foods

The availability of sensitive methods for detecting the carcinogenic polycyclic hydrocarbon, 3,4-benzpyrene (BP) has made it possible to look for this substance in soil, water and food. The fact that comparably sensitive

methods are not available for the detection of many other carcinogens has given BP a prominence which it probably does not deserve.

BP is present in a variety of cooked and uncooked foods. Bailey and Dungal (1958) found concentrations of between 0·3 and 2·1 μg per kg in Icelandic smoked meat and fish. Also, Lijinsky and Shubik (1964a; 1964b) reported concentrations of BP as high as 8 μg per kg in charcoal broiled steaks and smoked salmon. Gorelova and Dikun (1958a) reported even higher concentrations of BP in meat subjected to a 'home' smoking process for 3 months: sausages smoked in this way contained up to 10·5 μg per kg. The same authors (Gorelova and Dikun, 1958b) found that commercially smoked sprat contained up to 19·6 μg BP per kg. Davies and Wilmshurst (1960) reported the formation of 0·7 μg per kg in starch heated to between 370°C and 390°C, with temperatures of between 390°C and 400°C being recorded during the toasting of bread. Chassevent and Héros (1963) show there is little BP in commercially roasted coffee, but 'home' roasting processes include the endosperm, which is rich in BP.

Food may also be contaminated with BP from cigarette smoke and polluted air (Galuškinová, 1964). Gilbert and Lindsey (1957) record that BP is produced during the incomplete combustion of a variety of organic materials; for instance, it has been found in the smoke of both forest fires and garden bonfires. There is BP in minerals such as asbestos (Harington, 1965), in the soil (Kern, 1947; Blumer, 1961) and in water (Borneff, 1964); and as a result BP is present in many natural foodstuffs, both animal and vegetable. Borneff and Fischer (1962) found polycyclic hydrocarbons, including BP, in phytoplankton, a source of food for fish and whales. Therefore, no cooking or smoking process should be indicted as the source of BP in a foodstuff unless control measurements of BP in the raw food are also made. It is of interest that Jung and Morand (1962) found much less BP in refined olive oil than in fresh olives.

Other carcinogens, both polycyclic hydrocarbons (Lijinsky and Shubik, 1964b; Sepilli and Sforzolini, 1963) and carcinogens of other chemical types (for example, epoxides from heated fats: Seelkorf and Salfelder, 1962) have also been detected in food.

In Iceland the incidence of gastric cancer tends to be high and Dungal suggested an association with the consumption of smoked foods. Wynder and colleagues (1963) confirmed that in some areas of high stomach cancer incidence there exists a relatively high use of home-smoked or charcoal-broiled foods. However, no individual item of diet could be incriminated.

Field and Roe (1965) showed that single doses of BP (200 μg) alone, dissolved in polyethylene glycol, induced tumours of the forestomach epithelium in mice. However, no cancers of the glandular stomach equivalent to those seen in man, and no intestinal tumours, were encountered. Steiner, Steele and Koch (1943) fed or injected mice with various extracts from over-fried and over-baked meats: injection-site sarcomas were encountered in four mice but no gastro-intestinal tumours were observed.

The significance of these experiments with regard to human cancer is doubtful. Adenocarcinoma of the glandular stomach or colon are rare in small rodents. Either these species are not exposed to the relevant carcinogens, or they are naturally resistant to the induction of cancer at these sites.

If the latter is true, then these species are not suitable for the purposes of screening environmental agents for gastro-intestinal carcinogenicity.

Meanwhile, no harm can come from reducing exposure to BP in food. The smoking and processing of foods should be conducted under controlled conditions in factories. Genest and Smith (1964) found no BP in samples of cheese, wieners, or kippers smoked under controlled conditions, and Lijinsky and Shubik (1965) found no BP in preparations used to give a 'smoke' flavour to foods. Gretskaya and colleagues (1962) recorded that when foods are smoked by the burning of wood, in the presence of excess air, BP is confined to the particulate phase of the smoke and can be removed by filtration before coming into contact with the food.

Insecticides (DDT, Aldrin, Dieldrin and Aramite)

On the one hand, neoplasms of the liver have been seen in rats and mice after the feeding of various widely used chlorinated insecticides, including aldrin, dieldrin, DDT and aramite (Roe and Lancaster, 1964). On the other hand, the use of such agents has saved life and aided health (for example, in malaria eradication) and has helped to avert famine by making food production more efficient. Unfortunately, these compounds are very stable and their concentration has increased in human body fat (Hunter, Robinson and Richardson, 1963; Annotation, 1963). The average American consumed 0·2 mg DDT daily in 1945–46, the main source being animal fat (Durham and colleagues, 1961). Man can tolerate 35 mg DDT per day for up to 18 months without observable toxic effect (Hayes, Durham and Cipriano, 1956); but it is not known whether cancer will be induced after a longer exposure. The WHO Expert Committee on Pesticide Residues (WHO Expert Committee Report, 1964) recommended maximum daily intake levels calculated as one hundredth of the 'no-effect' level in the most sensitive species, the rat. Present day exposure levels are below these maxima.

Herbicides

Ethylcarbamate (urethane) is carcinogenic for a variety of tissues in different animal species (Tannenbaum and Maltoni, 1962). Urethane may initiate cancer induction in mouse skin so that subsequent treatment with a promoting agent, such as croton oil, elicits multiple tumours (Salaman and Roe, 1953). Carbamates related to urethane are useful as herbicides. Van Esch, van Genderen and Vink (1958) showed that two such compounds, isopropyl N-phenylcarbamate and isopropyl N-(3-chlorophenyl) carbamate were effective as tumour initiators in mice. Although there is no direct evidence that carbamates constitute a human cancer hazard, effective alternatives which are available for use should replace them.

Maleic hydrazide, used in agriculture to suppress plant growth and prevent the sprouting of potatoes, has proved carcinogenic when injected into rats (Dickens and Jones, 1965).

Hormones

Interference with normal homoeostasis by the administration or deprivation of hormones may predispose to cancer. The administration of goitrogens

may lead to thyroid cancer, and exposure to oestrogens may lead to cancer of various sites (Marois, 1964). Substances with oestrogenic, anti-oestrogenic, goitrogenic and other hormonal properties are present naturally in some foods. Foodstuffs may also become contaminated by oestrogens given deliberately to hasten growth in animals and by agricultural chemicals which have hormonal or anti-hormonal effects.

It is difficult to believe that ingested oestrogens are harmful under normal circumstances, since the levels in natural foods and oestrogen-fed animals are relatively low in relation to hormone secretion rates in man.

Masri and De Eds (1958) found that certain flavonoids affect hormone secretion by the pituitary and adrenal glands. Several vegetables have goitrogenic properties (Fertman and Curtis, 1951); and Clements and Wishart (1956) reported the presence of goitrogens in the milk of cows grazing on kale.

Detergents and Surface-active Agents

Surface-active agents are used in food processing, for example, as emulsifiers. Saffiotti, Shubik and Opdyke (1962) tested alkylbenzene sulphonate and an extract of alkylbenzenes for carcinogenicity on rabbit skin. The latter exhibited weak tumour promoting activity following initiation by a subcarcinogenic dose of 7,12-dimethylbenz[a]anthracene.

Water supplies have become contaminated with detergents; and there is evidence that the ingestion of detergents may aid the absorption of carcinogenic polycyclic hydrocarbons such as 3,4-benzpyrene from food, and thereby enhance the carcinogenic effect of such carcinogens on the stomach of small rodents (Borneff, 1963). However, positive results in animals were obtained with doses of detergent many times greater than those encountered in the normal human environment (Annotation, 1964).

Metals (Canned Foods)

Tin, of which cans are made, and lead in the solder with which they are sealed, find their way into the contents. Contamination takes place more easily in some foods, for example, milk and corned beef, and it occurs more quickly after the can is opened (Glassman and Barzutskaya, 1928). Lead is present in water, soils and plants, and tetraethyl lead in petrol has added to atmospheric pollution. Lead has induced kidney tumours in rats (Roe and Lancaster, 1964), but there is no known association between lead poisoning and cancer in man. Long-term feeding tests of tin compounds in rats and mice failed to reveal evidence of carcinogenicity (Walters and Roe, 1965; Roe, Boyland and Millican, 1965).

Inorganic arsenic is undoubtedly carcinogenic for man (Roe and Lancaster, 1964). Traces of arsenic are present naturally in food and levels are increased by the use of arsenical insecticides (Hoffman, Carson and Morris, 1963).

Selenium is both an essential nutrient and a potential carcinogen (WHO Expert Committee Report, 1961). Diets containing as little as 5–10 parts per million selenium produce cirrhosis and liver cancer in rats (Nelson, Fitzhugh and Calvery, 1943; Tscherkes, Volgarev and Aptekar, 1963).

Epidemiological studies suggest that the zinc/copper ratio in soil may have aetiological significance in relation to human stomach cancer (Stocks and Davies, 1964).

Sweeteners (Saccharin, Dulcin, Cyclamates, Sugars)

Fitzhugh, Nelson and Frawley (1951) induced liver tumours in rats by feeding the sweetening agent, dulcin. The same authors saw abdominal lymphosarcomas in rats fed saccharin, but doubted the significance of these results because a similar incidence of a thoracic form of the same type of tumour occurred in untreated control rats. Cyclamates were apparently without carcinogenic effect, though body growth was affected.

There are reports of induction of sarcomas in rats and mice by the injection of sugars, including glucose, fructose, maltose, lactose and sucrose. Hueper (1965), who failed to confirm these findings, suggested that the positive results obtained earlier may have been due to the presence of impurities in the sugars.

Food Colours

Some colour additives are of natural origin, but many are synthetic 'coal tar' colours, chemically related to substances of proven carcinogenicity. Several previously used food dyes, for example, butter yellow, were shown to be carcinogens. Hesselbach and O'Gara (1960) reported the induction of fibrosarcomas in rats at the site of injections of fast-green and light-green. Both dyes were used in food, drugs and cosmetics at the time. Also, Mannell and Grice (1964) saw rhabdomyosarcomas in two rats injected with blue VRS; and Mannell (1964) saw liver tumours in rats fed ponceau 3R. Other food colours, both synthetic and natural, have not been subjected to adequate long-term tests for carcinogenicity.

Flour Improvers

The use of agene was rightly curtailed on the grounds that it caused hysteria in dogs. Since bread is such an important item of the human diet, it was especially important that no chances be taken.

Long-term tests on azodicarbonamide, used extensively as a flour maturing agent, have revealed no suggestion of carcinogenic activity (Oser and colleagues, 1965).

Irradiation of Food

Food may be sterilized by high doses of ionizing radiation and irradiated foods have been examined for toxicity. Theoretically, carcinogens could be produced from inactive precursors by radiation. Toxic effects attributable to the destruction of thiamine, pyridoxine, and methionine have been noted (Brin and colleagues, 1961a; 1961b; Tsien and Johnson, 1959), but no increased tendency to cancer has been observed in animals fed irradiated foods (Radomski and colleagues, 1965).

Miscellaneous Hazards

The possibilities of contaminating food with carcinogenic chemicals are endless. Carcinogens in plastic wrappers, or in the lining of cans, can get

into food by elution. Printers' ink and dyes used in labelling may find their way into food unless precautions are taken, and accidental contamination may occur during storage or transportation. Substances such as ethyl alcohol, are considered elsewhere (*see* Chapter 12). For the rest, either extensive animal tests have revealed no hazard, or (and this is more usual) adequate tests have not yet been undertaken.

EXTRAPOLATION FROM THE LABORATORY TO THE HUMAN SITUATION

There are many examples of substances which have been shown to induce cancer in laboratory animals but not, as yet, in man. In most such instances circumstances have not arisen in which man is exposed to the same extent as animals under test. Arsenic is undoubtedly carcinogenic for man but has not yet been shown to be so for any other species. Many substances have been shown to be carcinogenic in one species of laboratory animal, but not in others. In the case of the potent carcinogens it is rare for the effect to be limited to a single species, but common for it to be limited to a particular organ (for example, the liver) irrespective of species.

As pointed out by Roe (1961), one would be concerned if one knew that exposure to an avoidable environmental hazard gave rise to cancer in 1 in 1,000, or even 1 in 100,000 persons at risk. It is impossible to detect such small risks by direct experiment in laboratory animals, and impossible or very expensive to detect them by epidemiological methods in man. Because of this difficulty it has become customary to reject as unsuitable for addition to food any substance for which there is any evidence of carcinogenicity in any species of animal. It has also become customary to test substances at dose levels much higher than those to which man is likely to be exposed. Few would disagree that this approach is reasonable in the case of substances which induce tumours in more than one species, or more than one tissue of the same species, following administration in doses and by routes which are not wildly unrealistic in relation to human exposure. Difficulties arise, however, where some of these conditions are not fulfilled. In particular, the relevance of subcutaneous injection tests of food additives and contaminants is open to question, as it is possible to induce sarcomas in rats and mice relatively easily by the injection of a wide variety of substances, many of which have not been shown to be carcinogenic following administration by other routes. However, the main purposes of subcutaneous tests of food additives and contaminants are, firstly, to pick up weakly carcinogenic agents with a view to testing them more extensively by other routes of administration, and secondly, to test for carcinogenicity, not at the site of injection but at other sites. There is a danger that failure to absorb materials from the gut reduces the real difference between the purposely high dose-level in feeding tests and the level which would mimic human exposure. Parenteral injection overcomes this problem. In order to avoid confusion which arises by the early induction of sarcomas at the site of injection, some have advocated spreading the total test dose through multiple subcutaneous sites.

Everybody concerned with food problems is aware of the difficulties of

extrapolation from animal experiments to man; but in most circumstances even a suspicion of carcinogenicity is enough to render the use of a food additive unwise.

LEGISLATION AND RESEARCH ON FOOD ADDITIVES AND CONTAMINANTS

In the United States of America (Report of Food Protection Committee, 1960), every new food additive is submitted to a set pattern of tests which include feeding it to dogs. In Great Britain, on the other hand (Report, 1960), a more flexible system of testing has been advocated. Both systems have been ably discussed elsewhere (Leading Article, 1961). In 1960, at a joint meeting of FAO (Food and Agricultural Organization of the United Nations) and WHO in Geneva, the evaluation of the carcinogenic hazards of food additives was discussed (FAO/WHO Report, 1961); and in subsequent publications the Joint FAO/WHO Committee made specific recommendations with regard to different classes of additives. Meanwhile, the European Economic Community (EEC) have set up a committee to consider the same problems.

At present, the control of new food additives is probably adequate, but a large-scale programme of testing traditional foods and additives for carcinogenicity is long overdue. Such a programme will demand a big increase in the availability of testing facilities such as those of the British Industrial Biological Research Association (BIBRA) and of trained staff. In recent years the Nuffield Foundation has taken a special interest in the subject through its Food Science Committee, and is currently offering Fellowships in Food Safety to medical, veterinary and science graduates.

GENERAL CONCLUSIONS

One may be fairly confident that in Great Britain no single food additive or food contaminant is having a major effect on the overall incidence of cancer. However, in the absence of further evidence from experimental studies, complete confidence is not justified, especially in the case of untested natural and traditional foodstuffs. It is very likely that factors present in food are involved in the aetiology of cancer of the oesophagus and liver in other countries (*see* Chapters 12 and 16) and much more attention should be directed to this aspect of cancer prevention.

Any proposal to expand the testing of food constituents for carcinogenicity should be viewed in perspective, as even the strictest legislation cannot hope to exclude all carcinogens from food. Some assessment of the extent of the possible risk to man is needed, and the effects of not banning a constituent must be weighed against the dangers of using a substitute or of using nothing. The problems of food production and preservation, famine, birth control and toxic effects of food constituents are interrelated. Carcinogenicity is by no means the only risk to health, and other hazards such as food poisoning, hepatotoxicity, lathyrogenicity, teratogenicity should be considered *pari passu*. In some parts of the world, life expectation is so short that the risk that cancer will develop later in life as result of substances present in food can command little serious attention.

Such a balanced view is only a matter of common sense. It is also a matter of common sense that, since even the strictest and most extensive tests in laboratory animals cannot exclude all possible hazards for man, all unnecessary additives should be excluded from foodstuffs.

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